REMARKS

Claims 18, 19 and 36 are currently pending and considered in the application. Claims 1-17, 20-35 and 37-104 claims have been withdrawn. Claim 18 is amended in the present response. Support for the amendments is found throughout the present application, for example at Paragraphs [0054] and [0056]. By these amendments, applicant does not acquiesce to the propriety of any of the Examiner's rejections and does not disclaim any subject matter to which Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

I. Claim rejections under 35 U.S.C. § 103

Claims 18, 19 and 36 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Leung et al, U.S. Patent No. 6,596,298, ("Leung") to Stanley et al, U.S. Patent No. 5,288,497 ("Stanley") and to Chobanian, U.S. Patent No. 6,139,847 ("Chobanian"); or alternatively, claims 18, 19 and 36 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Leung, in view of U.S. Patent Publication No. 2007/0184093, ("Hang") to Stanley and Chobanian; or alternatively claims 18, 19 and 36 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Stanley in view of any one of Leung in view of Hang and further in view of Chobanian. OA, pages 2-3.

The Examiner, argues that Leung "teach edible films that preferably include pullulan…the film more preferably comprises pullulan as a film forming agent in amounts of 45% to 70% ." OA, page 3. Regarding Hang, the Examiner argues that "Hang teaches soluble films comprising a soluble polymer and a strengthening polymer (0017) for delivery of emergency medical care active agents such as nitroglycerin (0019).... Leung or Hang fail to teach an embodiment containing nitroglycerin, in the claimed amount and lacks the combination with other cardiovascular agents." OA, page 3. The Examiner, however, argues that "Stanley teaches nitroglycerin in an amount of 0.4 to 1.0 mg (table 2, I 30-45), which is within the claimed 0.01 mg-100 mg of nitroglycerin." OA, page 4. The Examiner thus concludes "that it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to incorporate 0.4 to 1.0 mg of nitroglycerin of Stanley in the fast dissolving oral film containing pullulan of Leung or Hang because both Leung and Hang teach pullulan films for fast dissolution and for the delivery of oral active agents and

Hang particularly teaches the films for nitroglycerin delivery. Further, a skilled artisan would have been able to employ combinations of medicaments for treating cardiovascular conditions with an expectation to at least achieve an additional protective effect if not a synergistic effect, as suggested by Chobanian et al (abstract, col. 3-4)." OA, pages 4-5. Applicant respectfully traverses.

To maintain a proper rejection under 35 U.S.C. § 103, the Examiner must meet four conditions to establish a *prima facie* case of obviousness. First, the Examiner must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Examiner must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 947 F.2d 488, 493 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Examiner must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 175 F.3d 994, 999 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc.*, this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966). 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

Solely in the interest of advancing prosecution, and without agreeing with the propriety of the Examiner's rejection or disclaiming any subject matter to which they are entitled, Applicant has amended claim 18 as follows (additions underlined):

> A consumable film comprising nitroglycerin adapted to dissolve in the mouth of a patient, wherein said film comprises about 0.01 mg to about 100 mg nitroglycerin in a single layer including <u>about 40 to about 80 wt %</u> pullulan, <u>water in an amount from about 3 to about 8 wt %,</u> and at least one additional pharmaceutical agent, and wherein said consumable film is rapid-dissolving and provides rapid transmucosal delivery of nitroglycerin to a patient.

The cited references, Stanley, Chobanian Leung and Hang alone or in combination, do not teach or suggest each and every element of the presently-claimed invention. Speficically, the references, singly,or in combination, do not teach or suggest a consumable film including about 0.01 mg to about 100 mg nitroglycerin in a single layer consumable film including about 40 to about 80 wt % pullulan, water in an amount from about 3 to about 8 wt %, and at least one additional pharmaceutical agent, wherein the consumable film provides rapid transmucosal delivery of nitroglycerin to a patient.

"Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success…. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck,* 947 F.2d 488, 493 (Fed. Cir. 1991) (emphasis added) (internal citations omitted). In *In re Vaeck*, the PTO erred in rejecting applicants' claims as *prima facie* obvious wherein the prior art did not suggest the combination or convey to those of ordinary skill in the art a reasonable expectation of success of making it. *Id.* at 495. ("the prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art."). Accordingly, the Examiner must show where the prior art suggests a reasonable expectation of success of a consumable film that includes about 0.01 mg to about 100 mg nitroglycerin in a single layer consumable film, including about 40 to about 80 wt % pullulan, water in an amount from about 3 to about 8 wt %, and at least one additional pharmaceutical agent, wherein the consumable film provides rapid transmucosal delivery of nitroglycerin to a patient. This the Examiner cannot do.

Hang relates to producing "very strong films" (Paragraph [0032]) by adding strengthening polymers that "decrease the water solubility and total soluble matter of the end product" (*see, e.g.,* Paragraph [0033]). Specifically, Hang adds a second strengthening polymer to a soluble polymer that is provided in very small concentrations, *i.e.* concentrations of "0.1% to 5%." Paragraph [0029]. "The second polymer is a mechanically strong film

forming polymer or insoluble film forming polymer. In some embodiments, the second polymer is added at a concentration of 0% to 10%, in other embodiments, 0.1% to 10%, in yet other embodiments, 0.5% to 10% or in yet other embodiments, 1% to 10%." Accordingly, Hang relates to entirely different film compositions than the presently claimed invention. Hang relates to a strengthened film with far less polymer (such as pullulan) than the 40 to about 80 wt % pullulan in the presently claimed invention, and does not suggest any reasonable expectation of success of using or obtaining the claimed invention with the amount of nitroglycerin in a thin film comprising about 40 to about 80 wt % pullulan, and water in an amount from about 3 to about 8 wt % for rapid transmucosal delivery of nitroglycerin to a patient. As admitted by the Examiner, "Hang fail[s] to teach an embodiment containing nitroglycerin." *See* Final Office Action, mailed 9 September 2010 ("FOA"), page 3. Indeed, Hang does not relate to or indicate the use of or how to utilize a drug, much less nitroglycerin, in a consumable film comprising about 40% to about 80% pullulan (and other claimed ingredients) as presently claimed.

Stanley also does not teach or suggest a reasonable expectation of success of combining the elements as presently claimed. Regarding Stanley, the Examiner argues:

> Stanley teaches orally dissolvable medicaments wherein the composition is capable of absorption through the mouth, pharynx and esophagus (abstract), in particular for administering fast acting and potent drugs (col. 5, L 19-25). The medicament of Stanley involves a dissolvable matrix made of carbohydrates, fats or proteins (col. 5, L 43-52). For the active agents, Stanley teaches nitroglycerin in an amount 0 f 0.4 to 1.0 mg (table 2, I 30-45), which is within the claimed 0.01 mg-100 mg of nitroglycerin. Stanley lacks pullulan film and the combination of cardiovascular agents claimed.
>
> It would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to incorporate 0.4 to 1.0 mg of nitroglycerin of (Stanley) in the fast dissolving oral film containing pullulan of Leung or Hang because Stanley teaches the above amounts of nitroglycerin as appropriate for incorporating in a medicament matrix that enables fast absorption through mucosal membranes of oral cavity and over come the disadvantages of oral administration by other mechanisms such as frequent swallowing of pills, first pass effect, delay between the administration of tablets etc. Alternatively, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to prepare nitroglycerin dissolvable films with 0.4 to 1.0 mg of nitroglycerin of (Stanley) in the fast dissolving oral film containing pullulan of Leung or Hang because both Leung and Hang teach pullulan films for fast dissolution and for the delivery of oral active agents and Hang particularly teaches the films for nitroglycerin delivery.

OA, pages 4-5.

Stanley relates to lollipops that comprise drugs. *See* Stanley, Figs. 1-8. Stanley does not teach or suggest the use of thin films of any kind. The "dissolvable matrix made of carbohydrates, fats or proteins" in a lollipop does not have any relation to the consumable film with "about 40 to about 80 wt % pullulan" as presently claimed. Further, the Examiner's argument that Stanley demonstrates "orally dissolvable medicaments wherein the composition is capable of absorption through the mouth, pharynx and esophagus," apparently for nitroglycerin, is overstated. Stanley merely provides a laundry list of 72 drugs which includes nitroglycerin; there is no teaching or suggestion whatsoever regarding the use or utilization of nitroglycerin in thin films comprising about 40 to about 80 wt % pullulan water, much less in the described lollipops. Merely providing a laundry list of drugs (no matter the amounts) that may be included in lollipops, does not demonstrate to one of ordinary skill that there would have a reasonable expectation of success of making the invention as presently claimed.

Further, Leung and Chobanian fail to remedy these glaring deficiencies of Hang and Stanley as these references do not teach or suggest the limitation of a consumable film which provides rapid transmucosal delivery of nitroglycerin to a patient. Neither Leung nor Chobanian teach or suggest any range or amount of nitroglycerin.

In summary, there is simply no teaching or suggestion in the prior art of a consumable film about 0.01 mg to about 100 mg nitroglycerin in a single layer, about 40 to about 80 wt % pullulan, water in an amount from about 3 to about 8 wt %, and at least one additional pharmaceutical agent, wherein the consumable film provides rapid transmucosal delivery of nitroglycerin to a patient. Accordingly, Applicant respectfully requests that any rejections of pending claims under 35 U.S.C. § 103(a) over Leung to Stanley and to Chobanian, or over Leung, in view of Hang, Stanley and Chobanian, or over Stanley in view of any one of Leung in view of Hang and further in view of Chobanian., be reconsidered and withdrawn.

CONCLUSION

The Applicants have properly and fully addressed each of the Examiner's grounds for rejection. Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully submitted,

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